Environmental tobacco smoke (ETS) retention in humans from measurements of exhaled smoke composition.

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ABSTRACT

Twelve male volunteers were exposed for 60 minute periods to two concentrations of aged and diluted sidestream tobacco smoke (150 and 920 $\mu g.m^{-3}$ particulate), generated from a cigarette type, representative of middle-tar brands available in the UK, and at concentrations (for the lower level), similar to those reported from environmental surveys. Twelve female volunteers were exposed at the high level only. Measurements were carried out using an inhaled - exhaled technique.

For the twelve male volunteers, mean retention and standard deviation of particulate material as measured by UVPM (UV absorbance at 325 nm) the high and low exposure levels respectively were 41 ± 14% and 36 ± 20% (95% CI (higher level) : 30 - 50%), consistent with data from radiotracer studies (43 ± 17%) and from computer models of lung deposition for measured breathing patterns (34 ± 8%). Mean solanesol retention at the higher level exposure was 40 ± 20% (95% CI : 30 - 50%). Mean nicotine retention at the high and low exposure levels was 77 ± 17 % and 71 ± 12 % (95% CI : 62 - 88%), significantly greater than particulate retention.

For women, mean nicotine retention was 81 ± 16 % (95% CI : 70 - 91%), consistent with male data, but ETS particulate retention was significantly lower when measured by UVPM (17 ± 10% : 95% CI : 10 - 23%). Particulate retention as determined by solanesol measurements (27 ± 14% : 95% CI : 14 - 40%) was not significantly different from male values. The female particulate retention data were in agreement with model predictions of retention for measured breathing patterns (26 ± 5%).

High inter-subject variation was observed for both men and women for all three markers. In addition, the ratio of airborne particles to nicotine in the exposure chamber was variable

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with concentration, which is consistent with data from environmental surveys. It is concluded that these variations preclude calculations of particulate retention when only environmental nicotine concentrations are known, or when nicotine exposure has been extrapolated from biomarker data for nicotine or cotinine (a major nicotine metabolite).

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INTRODUCTION

Human exposure to environmental tobacco smoke (ETS) cannot be defined adequately in terms of exposure to airborne concentrations of ETS components alone as this is only one of many factors which affect the retention, and hence dose of these smoke components (McAughey *et al*, 1990). One of the most important of these additional factors is the degree of deposition of ETS particulate in the lung relative to more volatile ETS components. Using available data, particle deposition in the tracheo-bronchial region of the lung in passive smokers has been estimated as 0.02% that of mainstream smokers (McAughey *et al*, 1989), although this is dependent on the assumptions used and does not account for differences in chemical composition of the two smokes. One of the most important variables in this calculation is the fractional and regional deposition of particulate in the lung. The commonly used value of 10-11% total respiratory tract deposition is based on a single series of experiments by Hiller (1984). However, the measurement technique employed required that high concentrations of sidestream smoke be maintained, which was not representative of typical environmental exposures to ETS, where ageing and dilution effects are important in achieving an equilibrium ETS aerosol.

Nicotine and one of its principal metabolites, cotinine, have frequently been used as biological markers of ETS exposure. However, the physical and chemical behaviour of nicotine in ETS is not representative of other ETS components, and therefore, nicotine is likely to be a poor general marker (Eatough *et al*, 1989). This is confirmed by a recent publication which shows that the ratio of nicotine to both vapour- and particulate-phase components is highly variable (Nelson *et al*, 1992). A study by Iwase *et al* (1991) has measured retention of nicotine from ETS and shown retention fractions of 60 - 80 % (mean $\pm$ SD : 71.3 $\pm$ 10.2%) in a group of 17 non-smoking women inhaling sidestream

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smoke via an 'inhaled' minus 'exhaled' technique. However, particulate retention was not measured.

This study has enlarged the limited database of the proportion of the inhaled particulate phase of ETS which is retained by non-smokers, by measuring retention of specific components from aged and diluted sidestream smoke in male and female volunteers. The technique involves subtraction of exhaled quantities from quantities of the respective components inhaled. The measured components of the smoke aerosol were nicotine, UVPM (UV absorbance of a methanolic extract at 325 nm - a marker of ETS particulate (Conner *et al*, 1990)), and solanesol (a primary trisesquiterpenoid alcohol specific to the lipid fraction of tobacco leaves), which remains associated with ETS particulate as sidestream smoke ages and is diluted (Ogden and Maiolo, 1988). Exposures of all male subjects were carried out at two concentrations of ETS, the lower similar to values reported from environmental surveys, and a higher for improved confidence of analytical results above detection limits. Data from female subjects are available from exposures at the higher level only, as exhalate samples for UVPM and solanesol from the lower exposure concentration were below analytical detection limits, due to a combination of low ventilation rates in the female subjects.

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MATERIALS AND METHODS

Environmental Chamber

Atmospheres containing a surrogate ETS (aged and diluted sidestream smoke) were generated in a 14 m^3 chamber, in which temperature and humidity were controlled, and in which smoke concentrations were maintained at steady-state for 3 hours.

Smoke Generation

A detailed description of the smoke generation facilities may be found in Black *et al*, (1987). In brief, smoke was generated in a 0.4 m^3 glass-fibre glove box using a Mason-BAT smoking machine (Bevan, 1976) capable of smoking 1 to 12 cigarettes on a continuous cycle. The cigarette type used was typical of UK middle-tar brands. Sidestream smoke generated from the cigarettes was swept continually into the chamber by air diverted from the main inlet to the room, and then recombined with the main flow (Figure 1). Air from the glove box can also be fed directly into the laboratory extract, via a filter, to allow continuous control of the resulting smoke concentration. By varying the number of cigarettes, dilution of the smoke, and the air flow through the room, a wide range of concentrations can be achieved which represent a mix of fresh and aged smoke. Once equilibrium of carbon monoxide and particulate levels has been attained, volunteers can be introduced into the chamber via an airlock, thereby permitting exposures under constant conditions. Previous work has shown spatial mixing within the room to be good with a coefficient of variation for CO and particulate concentration at twelve sites within the room of 6.5% (Pritchard *et al*, 1988a).

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Exhaled Breath Capture System (Valving)

The system for collecting exhaled breath was based upon that developed for the exposure of volunteers to radioactive aerosols (Walsh *et al*, 1978 - Figure 2), although smaller exhalate filters were used in this study (90 mm reduced to 47 mm). The valving system comprised a breath (pressure) actuated Teflon™ shuttle valve, which moves between an inhale and exhale position. Breathing frequency, flow and volume were monitored on the inlet line via a pneumotachograph, with data handling and storage on a PC microcomputer. The exhalate line was attached, via an exhalate filter pack, to an external suction pump across a diaphragm valve, actuated by a pressure feedback loop, designed such that the volunteer felt no resistance to exhalation. The valve assembly was suspended from a counter-balanced pulley within the chamber, to permit the volunteers some freedom of movement. The mouthpiece of the valving assembly was modified to take an oro-nasal mask, part of which was occluded in order to reduce the dead-space in the breathing volume. Dead-space in the oro-nasal mask and valving assembly introduces potential errors into the measurement of retention, because the last part of an inhalation draws material into the valve assembly which never enters the respiratory tract. As soon as exhalation commences, this material is blown onto the filter. Similarly, at the start of inhalation, the initial material inhaled is the last part of the exhalate, which could be at a substantially lower particle and nicotine concentration than the chamber air. Thus, if the dead-space is large compared to the tidal volume, significant errors in the estimated retention occur. However, the effect of dead-space, and also any deposition in the valve assembly was accounted for mathematically. It has also been noted that during the finite time the valving system switches from inhale to exhale, some material may be re-exhaled through the inlet tube rather than to the exhale filter. This was measured and logged and was considered in the deadspace calculations for each subject.

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Mask fitting was checked during trial exposures, with the mask used having an air-filled sealing region to help fit by moulding to the face and the subjects taught how to check the seal. However, leakage remains a possibility during these long exposures. This was minimised by adjusting system flows across the exhalate diaphragm valve so that no resistance to exhalation was offered, and by being able to adjust suction during the exposure if the subject was aware of resistance changes on exhalation.

Exhale Filter Pack

The filter pack for the collection of exhalate comprised a 47mm diameter Teflon™ filter (Millipore, UK) to trap particulate material for subsequent analysis for UVPM and solanesol. This first filter was backed by a Teflon™ o-ring spacer, and a perforated Teflon™ sheet as a spacer. Another Teflon™ o-ring spacer was then used before a final 47 mm diameter glass fibre filter (Whatman, UK) impregnated with sodium bisulphate solution (4% w/v before drying), which was used to trap nicotine (Figure 2).

Room concentrations of UVPM and solanesol were measured by collection onto a 25 mm diameter Teflon™ filter (Millipore, UK) with nicotine collected separately on XAD-4 adsorption tubes (SKC, UK).

Chamber Monitoring

A number of methods were used to monitor the chamber atmospheres in real time, in addition to UVPM, solanesol and nicotine sampling. Carbon monoxide was measured with an electrochemical cell (Bedfont, UK), ETS particulate concentration was monitored with a MiniRam (calibrated for ETS measurement), and particle number was determined using

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a condensation nucleus counter (CNC-TSI, USA). Further particle analysis and sizing were carried out using a Las-X laser spectrometer (Malvern, UK) based on light scattering and a quartz crystal microbalance (QCM - Berkeley Telonic, UK). Flow rates for all sampling equipment were measured before the start of each run using an bubble flow meter which electronically times the passage of a soap film across a fixed volume (Gilibrator, Gilian, USA).

ETS Particulate - Chamber

ETS particulates were collected in the 14m^3-chamber during each volunteer exposure by sampling onto two 25 mm diameter Teflon™ filters at two measured flow rates of approximately 5 and 15 Lmin^{-1} respectively for the duration of the 60 minute volunteer exposure. The tar from each filter was dissolved in 5ml methanol and its UV absorbance measured at 325 nm. The ETS particulate concentration was then calculated from a calibration curve of UVPM (absorbance at 325nm) versus mass, from a calibration prepared from serial dilutions from ETS particulate samples of known dry mass.

ETS Particulate - Exhaled

Tar from the 47 mm diameter Teflon™ exhalate filter was dissolved in 5ml methanol and the UV absorbance measured at 325 nm. The exhaled particulate was then calculated from a calibration curve of UVPM (absorbance at 325nm) versus dry mass and corrected for dead space effects. Previous measurements had determined that the slope of the calibration curve for exhaled measurements was not significantly different for that obtained from ETS measurements in the chamber.

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Solanesol

The methanol extracts used for UVPM measurements were also used for solanesol analysis by reverse phase HPLC (Waters Resolve C18 : 15cm, particle diameter 5 micron, pore diameter 90 Angstrom). The flow rate (100% methanol solvent) was 1 $ml.min^{-1}$, the injection volume 100 µl and solanesol was detected by UV absorption at 210 nm. Solanesol was quantified by reference to a prepared standard curve (Solanesol : Sigma S7854) over the range 0.125 to 1.0 $\mu g.ml^{-1}$. The limit of detection for solanesol was 0.05 $\mu g.ml^{-1}$, with a between-run precision of 6.9%. All samples were analysed in duplicate. It should be noted that a high degree of variability was seen in the HPLC traces for solanesol analysis, with differing degrees of complexity. This often required the solanesol concentration to be calculated from a sloping baseline or as a shoulder peak.

Nicotine - Chamber

Nicotine samples were collected from the chamber during the 60 minutes of each run using XAD-4 adsorption tubes (SKC, UK, (Hammond *et al*, 1987, Ogden, 1989)). Two samples were obtained, each with a measured sampling rate of approximately 4 $l.min^{-1}$. The tubes were eluted using 2 ml ethyl acetate containing 0.1% w/v triethylamine with 0.909 $\mu g.ml^{-1}$ quinoline as an internal standard. Samples were analysed on a HP 5890 GC with NP detection. Two µl of sample were injected onto the column of RTX-5 (30m x 0.32 mm id with 1 µm film thickness).

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Nicotine - Exhaled

The acidified, bisulphate-impregnated glass fibre filter was extracted with a mixture of 5M sodium hydroxide (20 ml) and di-isopropyl ether (50 ml). Quinoline (1.05 $\mu g.ml^{-1}$) was used as internal standard with subsequent GC/NPD analysis as above.

Volunteers

Twelve male and twelve female volunteers, all non-smokers, were recruited by advertisement from the workforce at the Harwell Laboratory, following approval of the study by the AEA Technology Ethical Committee. Each volunteer was interviewed and examined by a medical practitioner to determine fitness to participate, and each performed a vitalograph test to determine lung capacity. An informed consent for participation in the study was then obtained from each volunteer.

Each subject was given training on the valving apparatus in the absence of smoke in the chamber, for at least 15 minutes. On separate days, each male subject participated in a low- and a high-level exposure of 60 minutes; each female was subject to a high level exposure only. Subjects were exposed singly or in pairs within the chamber, where two sets of valving apparatus were available. All subjects were asked to minimise their ETS exposure prior to each experiment, although the workplaces of the majority of the subjects were non-smoking areas.

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RESULTS

Chamber Monitoring

All measurement methods used demonstrated that following an equilibration period, steady-state concentrations of aged and diluted sidestream smoke could be maintained over periods of several hours. Figure 3 shows particle (CNC) and mass (MiniRam) concentrations measured during typical high and low level exposures. Volunteers exposures in each case took place during the period between 30 and 90 minutes as shown in Figure 3. A mass median diameter (MMD) of 0.14 µm (σ_g = 2.6 : n = 5) was measured using the quartz crystal microbalance (QCM), in effect a cascade impactor with cut-off stages of 0.1, 0.2, 0.4, 0.7, 1.1, 2.0, 3.6, 7.0, 12.0, and 24.8 µm. A count median diameter (CMD) of 0.125 µm (σ_g = 1.5 : n = 20) was measured using the Las-X spectrometer, with particle counts measured in the 0.11, 0.15, 0.2, 0.25, 0.3, 0.4, 0.5, 0.65, 0.8, 1.0, 1.25, 1.5, 2.0, 2.5 and 3.0 µm cut-off regions.

Exposure Concentrations

Mean UVPM, solanesol and nicotine concentrations at the various exposure levels are shown in Table 1. The low level exposure is at levels higher than, but of the same order of median values reported from environmental surveys reviewed in the literature (e.g. Guerin *et al.* 1992). The higher level exposures were carried out such that concentrations of the exhaled components captured in the filter pack would be significantly greater than the detection limits for the appropriate analytical techniques, so that improved analytical precision would be achieved. The lower level measurements, at concentrations approaching analytical detection limits, could then be assessed critically.

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Solanesol levels are approximately 1.3% of total particulate levels, consistent with literature data (Ogden and Maiolo, 1988). It was observed that there was a greater variation in nicotine concentrations than was seen for the corresponding ETS particulate and solanesol measurements. This was reflected in the particulate / nicotine ratio measured in the chamber (Table 1 and Discussion).

Details of the volunteers are listed in Table 2. There was no significant difference in age between the two groups, but the men were significantly taller and had significantly greater Forced Vital Capacities (FVC - a measure of lung volume). Both groups showed increased vital capacities over the expected norm for age and height, reflecting a 'healthy worker' effect in recruitment for the study.

Retention

A summary of retention of each measured component in the respiratory tract is shown in Table 3. The summary table lists Mean Retention ± Standard Deviation for the group. Predicted retention values for particulates using a model of respiratory particle deposition (LUDEP - Birchall, 1991) are also shown. Standard errors were approximately 5% for high level exposures and 10-15% for male, low level exposures arising principally from the component concentrations of the exhalate being close to the analytical detection limits.

The retention of ETS particulate (as UVPM) in the male volunteers is consistent at both high and low level exposures, with a mean retention fraction of 41 ± 14% for high level exposures (95% CI = 31 - 50%) and 36 ± 20% for low level exposures (95% CI = 20 - 52%). Retention in females assessed by UVPM was found to be significantly lower than

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that for men with an average retention of 17 ± 10% (95% CI = 10 - 23%) at the higher level.

No solanesol results have been reported from the low level exposures for men and women, as exhaled solanesol levels were approaching the detection limit of the assay, yielding absolute errors of ± 15 - 60%. At the high exposure level, mean retention fractions of 40 ± 20% for men (95% CI = 30 - 50%) and 27 ± 14% for women (95% CI = 14 - 40%) were observed. Thus, solanesol retention for male volunteers is in agreement with the UVPM values. HPLC assays for solanesol from 4 exhaled filters from females (A, B, F and L) and 2 for male subjects (D and J) gave complex traces over high and rising baselines, in which it was difficult to determine peak areas accurately, in contrast to the majority of analyses where normal baselines were achieved. These outliers suggested solanesol retentions of << 0% or > 100%. These data were excluded from the summary table calculations (Table 3), being rejected on the grounds of unsatisfactory resolution of the HPLC traces.

Mean fractional nicotine retentions of 77 ± 17% and 71 ± 12% (95% CI = 62 - 88%) were seen for the male group of volunteers under the high and low exposure conditions respectively. Retention in the female group of volunteers was 81 ± 16% (95% CI = 70 - 91%) at the high exposure level.

Average breathing patterns for the volunteer groups (Table 4) show that there was consistency in breathing pattern for high and low level exposures. In general, men took larger breaths but fewer of them, reflecting their larger lung capacity. Both male and female volunteers, on average, used only 17% of their lung capacity during the breathing cycle of the experiment. This is consistent with breathing at rest, and implies that the subjects did not have to make efforts to exhale forcibly.

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DISCUSSION

Male Volunteers

The results obtained for retention of ETS components in male volunteers show a consistent pattern. For particulates as UVPM, mean retention was 41 ± 14% and 36 ± 20% of that inhaled at the high and low exposure levels respectively, and this was confirmed by results for solanesol. These data are higher than previous assumptions made for particulate retention of 11 ± 4% (Mean ± SD) as reported by Hiller (1984). However, the deposition fractions reported by Hiller were for 0.41 µm mass median aerodynamic diameter (MMAD) smoke particles rather than the 0.14 µm MMAD particles reported in this study. Other recent studies in which ETS particle size has been determined in laboratory situations report ETS particle size at 0.15 - 0.25 µm MMAD at ETS concentrations typical of environmental exposure (Guerin *et al*, 1992). Thus lung deposition models would predict deposition fraction to be greater than those measured by Hiller as deposition by Brownian motion becomes more significant at the lower particle sizes (ICRP, 1966).

Model predictions of particle deposition were calculated to be 34 ± 8% applying each person's measured breathing pattern in the LUDEP lung model (Birchall *et al*, 1991), although no significant correlation was found for observed versus predicted values for UVPM or solanesol. Using the LUDEP model for the experimental conditions reported by Hiller, a deposition fraction of 22% was obtained. In each case, predicted extra-thoracic deposition is negligible, irrespective of mouth or nasal breathing, suggesting that total retention is approximately equivalent to lung deposition.

The experimental data are consistent with those from another study (Strong *et al*, 1993) in which total and regional deposition of ETS were measured using exhale capture

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techniques plus a radiotracer (^{212}Pb) attached to the involatile particulate, allowing whole body monitoring for retention and excretion measurements. Total retention was 43 ± 17% (Mean ± SD) for a group of nine male volunteers following a fixed mouth breathing pattern of 6 x 1.0 litre breaths per minute, which was very close to the mean pattern seen for the male volunteers in this study. The inter-subject variation observed in this study was similar to that reported by Strong *et al*, 1993 and Hiller, 1984, although greater than predicted by the model (Birchall *et al*, 1991).

Particulate retention data for female volunteers are less clear-cut than the data for the males. Retention fractions for solanesol and UVPM were approximately 27 ± 14 % and 17 ± 10% respectively. The LUDEP particle deposition model with measured breathing patterns predicted particle deposition of 26 ± 5% (Birchall *et al*, 1991) and a significant correlation was observed for observed particulate deposition (UVPM) versus predicted (LUDEP) values ($p<0.001$). Inter-subject variation was similar to that observed for male subjects. Although nicotine retention data for the female group were satisfactory, only 67% of the female volunteers gave reproducible results for solanesol. It was initially assumed that solanesol data exhibiting a retention of less than 0% were a consequence of problems in exhalation and mask fitting; while this is possible in some cases, such an effect would not explain why the majority of the nicotine retention results for the group were reproducible. Both men and women, were breathing to only 17% of their vital capacity during the experiments, suggesting that no discomfort was experienced. Analytical blanks for all analytes were satisfactory for chamber and exhalate generated samples, although complex baselines on a number of solanesol HPLC assays made interpretation difficult. Hence summary data in Table 3 excludes the outliers where $0\% > x > 100\%$.

It is possible that the problems encountered with the assays for solanesol for female exhalate may arise from a gender difference. Similar anomalies were observed for UVPM

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measurements in preliminary exposures for women with deposition values << 0%. Generally, women have a higher proportion of adipose tissue in body composition, and that this may act as a depot for organic molecules. Thus, release of these components may differ from men and account for measurement differences in the presence of ETS, as blanks were unaffected.

Although mean ETS particulate retention for each gender is greater than the value of 11% reported by Hiller, 1984, it should be noted that total intake of ETS particulate remains low. Many authors have used the concept of 'cigarette equivalents' in order to give a measure of dose relative to the dose from a single cigarette in an active smoker. By assuming toxicological equivalence of the two smokes, risk estimates have been constructed. Estimates of 'cigarette equivalents' have varied from 0.024 to 27 cigarette equivalents per day, a range which has been seen as illogical (US Department of Health and Human Services, 1986). Calculations for the highest estimate in this report divided the calculated ETS particulate intake by a mainstream smoke intake of 0.55 mg per cigarette, a minimum yield value for cigarette brands available in the US. However, the original authors of the cited work quote a sales weighted average mainstream smoke yield of 17 mg per cigarette (Repace and Lowrey, 1980). Use of this more realistic value would reduce the range quoted in the US Surgeon General Report to 0.024 to 0.9 cigarette equivalents per day. While early estimates based ETS dose on ETS concentration per unit volume multiplied by volume inhaled, more recent calculations of ETS dose have taken into account deposition fraction and adjusted exposure via time-activity matrices which estimate the duration of exposure, at work and/or home, with ventilation volumes adjusted for activity such as light work or exercise (Holcomb, 1993). On this basis, Holcomb has calculated daily ETS particulate intake under a variety of lifestyles, with maximum intakes of 109 $\mu g.day^{-1}$ for men and 58 $\mu g.day^{-1}$ for women, and 45 and 34 $\mu g.day^{-1}$ respectively for home and leisure exposure only. However, exposure concentrations were based on

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attributing specific ETS exposure to the difference in particulate concentration between smoking and non-smoking areas. The values obtained are in contrast to mean and maximum ETS particulate intakes of 1430 and 14 300 $\mu g.day^{-1}$ respectively, which represent the maximum reported literature values as calculated by Repace and Lowrey, 1980.

ETS particulate intake has been calculated for home and workplace using the deposition and ventilation data measured in this study with with exposure concentrations based on those suggested by Holcomb (1993). Summarising likely exposure, Holcomb uses a series of studies carried out in the US and Canada, suggesting that the difference in mean RSP or UVPM measurements for smoking (S) and non-smoking (NS) areas were 27 $\mu g.m^{-3}$ for homes (50S v 23NS), 22 $\mu g.m^{-3}$ for offices and public places (68S v 46NS), 42 $\mu g.m^{-3}$ for restaurants (132S v 90NS), 30 $\mu g.m^{-3}$ for trains (216S v 186NS) and 104 $\mu g.m^{-3}$ for bars and taverns (S data only), and that these differences relate to exposure attributable to ETS. Our calculations have been carried out using both the absolute mean particle concentrations in smoking areas (S) and the difference between smoking and non-smoking areas (S-NS), which Holcomb attributes to the ETS component of the ambient particulate. Thus, absolute (S) values will give a maximum value for intake from total particulate exposure.

In our calculation, a 16 hour exposure at the ventilation rates measured during the study is assumed (0.42 m^3 per hour for men and 0.36 m^3 per hour for women). Workplace exposure assumes an 8 hour exposure at twice the resting ventilation rate. Fractional deposition values were 0.41 for men and 0.27 for women, and the calculated values are shown in Table 5. Values are higher than those reported by Holcomb (1993) reflecting the increased deposition fraction used in our study, although measured ventilation rates in our work were lower than the equivalent values used by Holcomb.

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It has been reported that the fractional deposition of mainstream tobacco smoke is greater than for ETS with values ranging from 47 - 90% (US Surgeon General, 1986) with most reported values at the higher end of this range. Measurements of tar deposition in mainstream cigarette smokers using radiotracers have shown an intake of 453 mg per day (range = 307 - 728 mg per day) in male middle-tar smokers with an average intake of 13.5 mg per cigarette (range = 7.4 - 22.0 mg per cigarette) (Pritchard *et al*, 1988a, McAughey *et al*, 1989). Equivalent data for female smokers give values of 284 mg per day (range = 111 - 488 mg per day) and 12.5 mg per cigarette (range = 9.3 - 21.2 mg per cigarette) (McAughey *et al*, 1991). In each case, the mean delivery of the cigarette was equivalent to the Sales Weighted Average Tar for the UK, consistent with the measured yield of the experimental cigarette. Cigarette equivalent data and daily intake as a fraction of mainstream intake are shown in Table 6, confirming that average doses from ETS are small.

Althogh the nature of this study was such that regional deposition could not be measured, regional deposition data (Strong *et al*, 1993) for ETS particulate using a radiotracer suggests that the regional deposition patterns of mainstream tobacco smoke and ETS particulate are different, with ETS particulate depositing more deeply in the lung. Therefore, direct comparisons of particulate retention on a cigarette equivalent basis may be inappropriate. This concern is supported by the US Environmental Protection Agency, who chose not to consider the use of 'cigarette equivalents' in their recent publication reviewing the respiratory health effects of passive smoking (USEPA, 1992) for a variety of reasons. For example, although mainstream tobacco smoke (MS) and ETS are qualitatively similar with respect to chemical composition, the absolute and proportional quantities of the smoke components, their physical state and their partitioning between phases can differ. Further differences included variations in particle size between MS and

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ETS and different breathing patterns in smokers and non-smokers, leading to differences in the distribution and deposition of each type of smoke in the respective populations. Subsequent metabolic differences were also discussed, suggesting dose-response associations were likely to be non-linear.

Nicotine retention in men and women was significantly different from particulate retention, with observed mean retention values of 70 to 80%. This is consistent with data from a study by Iwase *et al* (1991) which measured retentions of nicotine of 60 to 80% (mean ± SD. 71.3 ± 10.2%) in a group of 17 non-smoking women inhaling sidestream smoke. Data were obtained by a similar inhaled minus exhaled technique to that reported here, but using nicotine denuders rather than a bisulphate impregnated filter.

However, these data confirm that nicotine retention is not a representative marker of ETS exposure. This is particularly important with respect to a recent publication (Nelson *et al*, 1992) which suggests that the ratio of nicotine to both vapour- and particulate-phase components is highly variable with respect to sampling time and ventilation. Thus, environmental surveys of nicotine exposure will be of greater variability than our data and those of Iwase *et al* (1991), which also represent a steady state situation.

The ratio of airborne particulate to nicotine in the exposure chamber was significantly different at the two exposure levels in this study (Table 1). This is consisent with previous data in which the ratio of particulate nicotine / vapour nicotine increased with particulate concentration (Guerin *et al*, 1992). This pattern is consistent with a dynamic reversible equilibrium of nicotine between vapour and particulate phases. In this study, and in most environmental studies, only nicotine vapour was measured.

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These data support the conclusion of Nelson *et al*, 1992, suggesting that nicotine intake cannot be related directly to particulate intake. The variability of particle / vapour ratio precludes calculations of particle retention when only environmental nicotine concentrations are known, or when nicotine exposure has been extrapolated from bioassay data for nicotine or cotinine (a major nicotine metabolite).

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Figure 1 - Exposure system

Figure 2 - Valve and exhale capture system

Figure 3 - Maintenance of steady-state ETS concentrations

Figure 4 - Retention Data (Male Exposures)

Figure 5 - Retention Data (Female Exposures)

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Source: https://www.industrydocuments.ucsf.edu/docs/mgnm0000

Table 1 - ETS exposure levels

Experiment	UVPM Mean ± SD ($\mu g.m^{-3}$)	Solanesol Mean ± SD ($\mu g.m^{-3}$)	Nicotine Mean ± SD ($\mu g.m^{-3}$)	UVPM/Nicotine Ratio Mean ± SD
Male, High level (n=12)	920 ± 120	11.7 ± 1.5	29 ± 13	31.7
Male, Low level (n=10)	150 ± 60	1.5 ± 0.7	9.5 ± 2.3	15.8
Female, High level (n=12)	1040 + 140	13.2 ± 3.2	35 ± 10	29.7

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Source: https://www.industrydocuments.ucsf.edu/docs/mgnm0000

Table 2 - Volunteer data

Subject	Male (n=12) Mean ± SD (Range)	Female (n=12) Mean ± SD (Range)
Age (y)	33 ± 5 (26 - 45)	33 ± 10 (22 - 51)
Height (m)	1.76 ± 0.05 (1.68 - 1.85)	1.65 ± 0.06 (1.57 - 1.77)
FVC (l)	5.82 ± 0.74 (4.78 - 7.29)	3.95 ± 0.72 (2.82 - 5.20)
FVC/Norm (%)	118 ± 18 (98 - 160)	112 ± 17 (86 - 136)

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Source: https://www.industrydocuments.ucsf.edu/docs/mgnm0000

Table 3 - ETS Retention

Condition (No. of subjects)	Male Retention ± SD (%) (Range)	Female Retention ± SD (%) (Range)
UVPM High (12M, 12F)	41 ± 14 (12 - 65)	17 ± 10 (3 - 39)
UVPM Low (10M)[a]	36 ± 20 (5 - 65)	-
Solanesol High (10M, 8F)[b]	40 ± 20 (20 - 57)	27 ± 14 (10 - 58)
Nicotine High (12M, 12F)	77 ± 17 (41 - 100)	-
Nicotine Low (10M)[a]	71 ± 12 (49 - 88)	81 ± 16 (39 - 96)
Predicted particulate retention (LUDEP)	34 ± 8 (28 - 50)	26 ± 5 (20 - 39)

[a] 2 male subjects declined to undertake low level exposure

[b] excluding values of << 0% or > 100%

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Source: https://www.industrydocuments.ucsf.edu/docs/mgnm0000

Table 4 - Breathing Patterns

Condition	Male, High Level Mean ± SD (Range)	Male, Low Level Mean ± SD (Range)	Male, High Level Mean ± SD (Range)
Volume (l)	439 ± 119 (226 - 647)	422 ± 86 (326 - 629)	358 ± 122 (242 - 606)
Number of Breaths	490 ± 170 (187 - 766)	450 ± 133 (254 - 726)	566 ± 154 (307 - 802)
Volume per Breath (l)	0.98 ± 0.33 (0.46 - 1.74)	1.02 ± 0.31 (0.48 - 1.53)	0.66 ± 0.21 (0.40 - 1.02)
%FVC per Breath	17 ± 8 (8 - 36)	17 ± 6 (8 - 32)	17 ± 5 (10 - 27)

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Source: https://www.industrydocuments.ucsf.edu/docs/mgnm0000

Table 5 - Estimated ETS / Particulate Intake

Condition	Particle Concentration ($\mu g.m^{-3}$)	Exposure Duration (h)	Ventilation ($m^{-3}.h^{-1}$)	Deposition Fraction	Particulate Intake ($\mu g.day^{-1}$)
Home					
Male (S)	49	16	0.42	0.41	135
Male (S-NS)	27	16	0.42	0.41	74
Female (S)	49	16	0.36	0.27	76
Female (S-NS)	27	16	0.36	0.27	42
Work					
Male (S)	68	8	0.84	0.41	187
Male (S-NS)	22	8	0.84	0.41	61
Female (S)	68	8	0.72	0.27	106
Female (S-NS)	22	8	0.72	0.27	34

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Table 6 - Comparison of particulate intake from cigarette smoking and exposure to ETS

Exposure Condition	Particulate Intake ($\mu g.day^{-1}$)	Daily intake as % smoker intake	Daily Cigarette Equivalent
Home			
Male (S)	135	0.030	0.010
Male (S-NS)	74	0.016	0.005
Female (S)	76	0.027	0.006
Female (S-NS)	42	0.015	0.003
Workplace			
Male (S)	187	0.041	0.014
Male (S-NS)	61	0.013	0.005
Female (S)	106	0.037	0.008
Female (S-NS)	34	0.012	0.003

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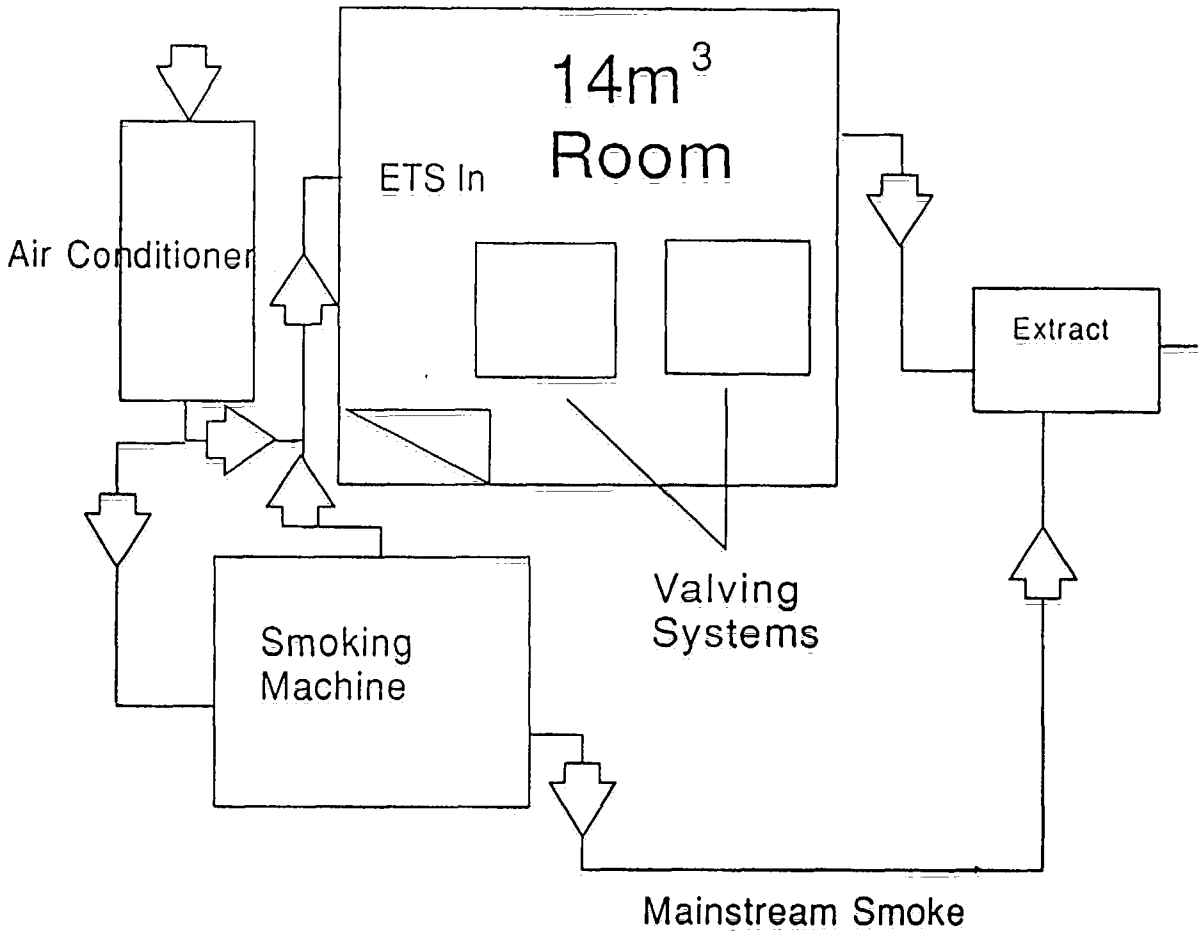
Source: https://www.industrydocuments.ucsf.edu/docs/mgnm0000



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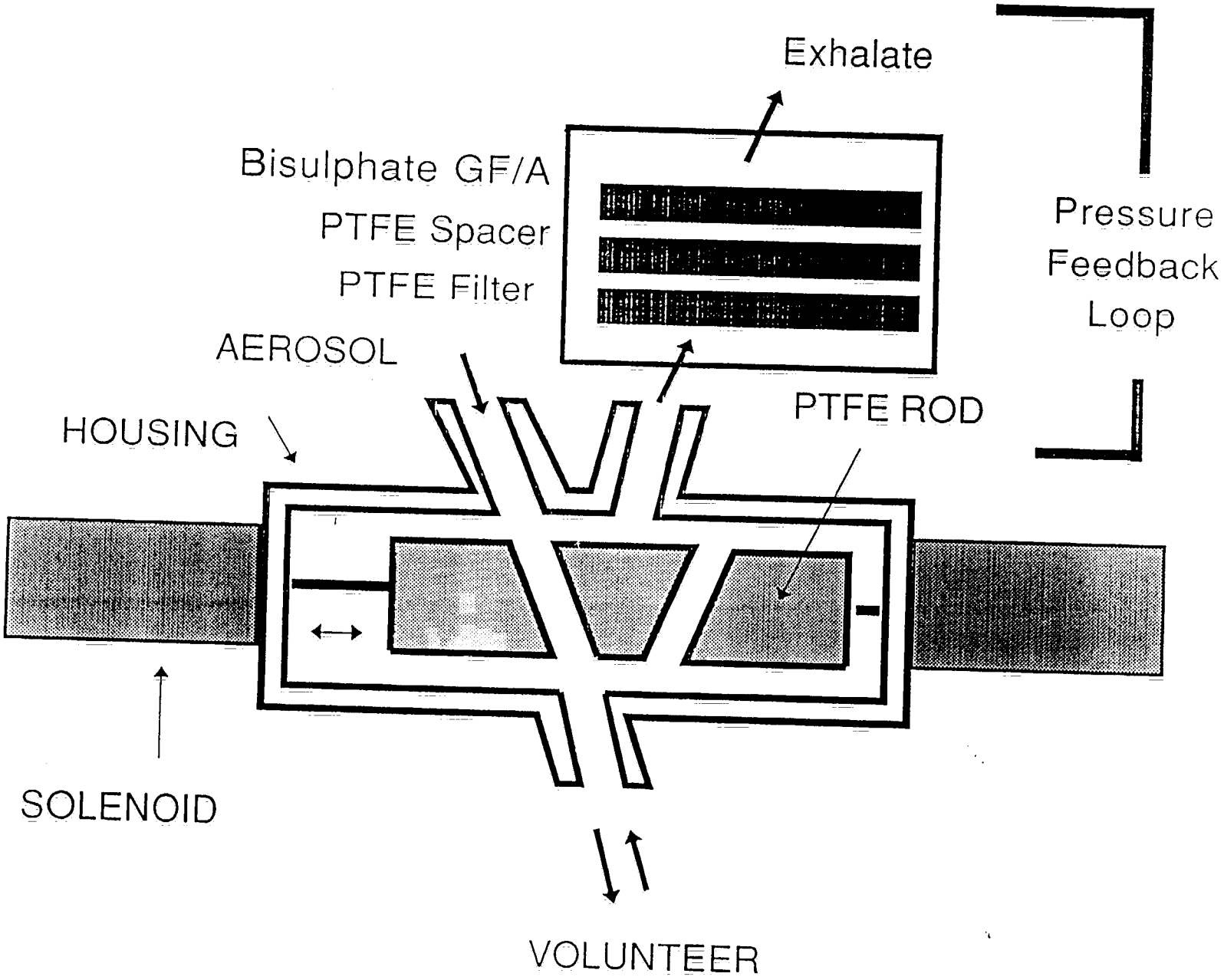
Source: https://www.industrydocuments.ucsf.edu/docs/mgnm0000



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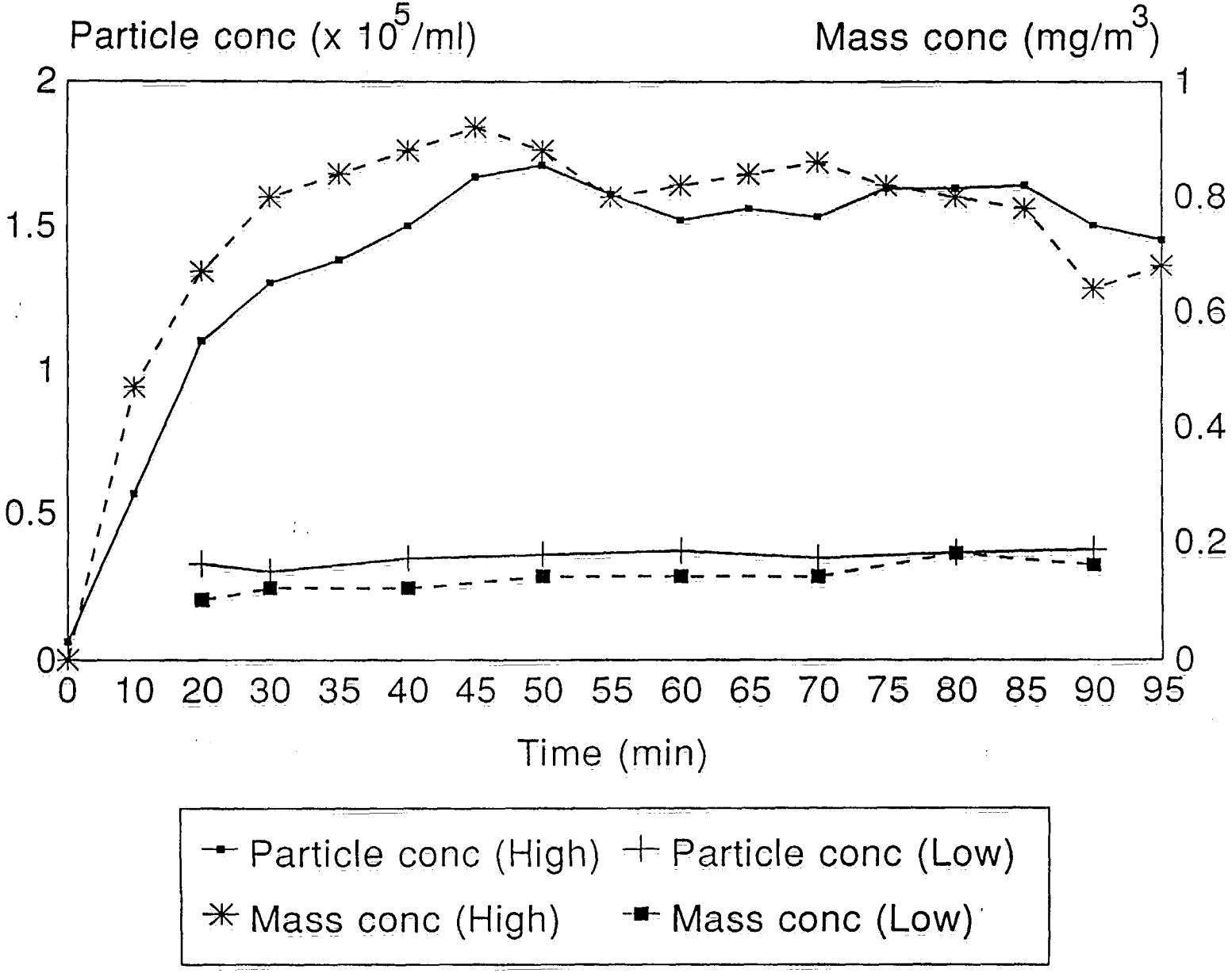

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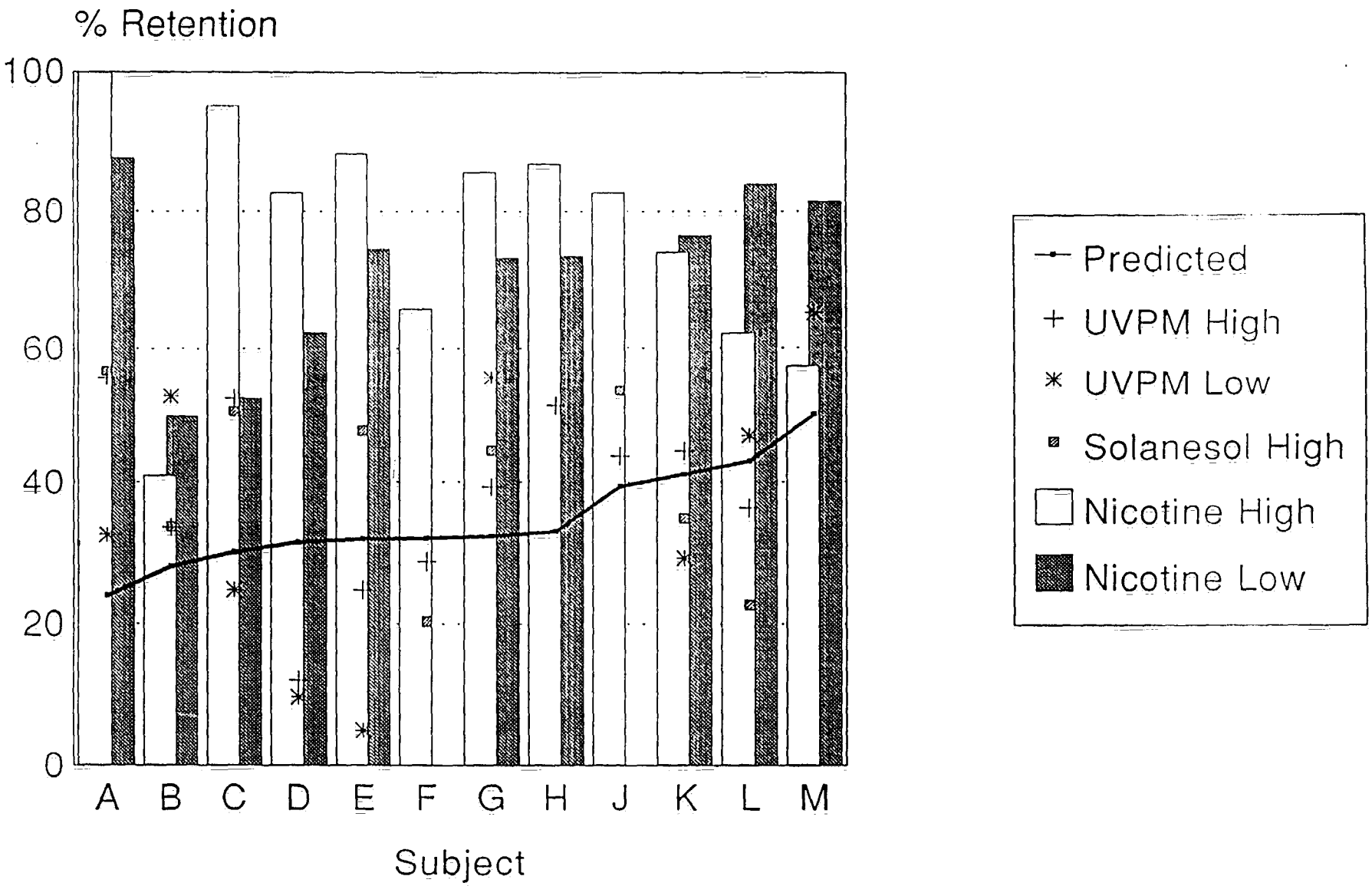

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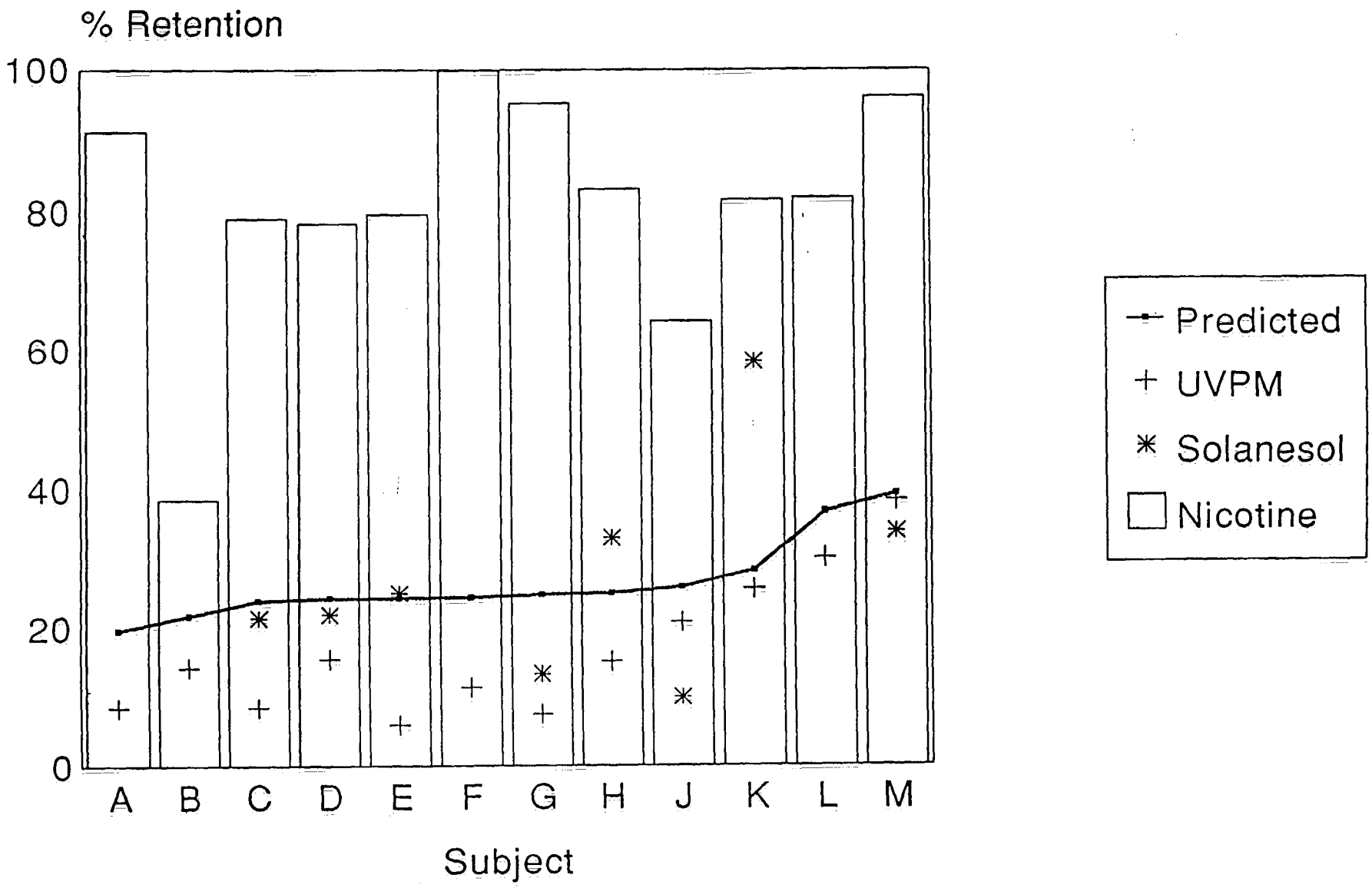

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